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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
01/13/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/560,829	ISHIKAWA ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,2,4-24,27 and 34-38* is/are pending in the application.

4a) Of the above claim(s) *9-24 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8 and 34-38* is/are rejected.

7)☒ Claim(s) *1,2,4-8 and 34-37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/18/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Status

Applicants' response dated October 14, 2008, to the non-final action dated April 15, 2008, has been entered. Claims 1, 2 and 4-8 have been amended. Claims 3, 25, 26 and 28-33 were cancelled and claims 34-38 were newly added. Accordingly, claims 1, 2, 4-24, 27 and 34-38 are pending in the application. Claims 9-24 and 27 stand withdrawn from further consideration, with traverse, as drawn to non-elected inventions and species of the invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01. The claims have been examined commensurate in scope with the elected species of the invention, i.e. mouse and immunoglobulin G.

Claims 1, 2, 4-8 and 34-38 are under current examination.

Information Disclosure Statement

The information disclosure statement filed 8/18/2008 is in compliance with 37 CFR 1.98(a); thus the information contained therein has been considered and indicated as such on form PTO/SB/08a.

Response to Objection to Specification

The brief description of the drawings corresponding to Figures 1-12 were objected to in the previous office action dated April 15, 2008. Applicants have amended the brief description of the Figures, obviating the grounds for objection. Thus, the objection is hereby withdrawn.

Response to Claim Objection

Claim 1 was objected to for employing incomplete sentence structure, in the previous office action dated April 15, 2008. Applicants have amended the claim to correct the deficiency. Accordingly, the objection is hereby withdrawn.

New Claim Objections

Claims 1, 2, 4-8 and 34-37 are newly objected. The claims have been amended so as to be directed to a NOD/SCID/IL2rg-null mammal (excluding human). Although the examination of the instantly claimed invention has been limited to the elected species of mouse, it should be noted that the NOD/SCID genotypic designation is reserved for mice, and is not generally applicable to other mammals. Moreover, the instant specification defines the extended genotypic designation NOD/SCID/IL2rg-null as that of NOD.Cg-*Prkdc*^{scid}IL2rg^{tm1Wjl}/Sz mice. The claims should therefore be amended to recite a NOD/SCID/IL2rg-null mouse.

Priority

This Application claims the benefit of foreign priority under 35 U.S.C. 119(a)-(d), to Japanese Application 2003-171240 (6/16/2003). However, it is noted that Applicant cannot rely upon the foreign priority papers to overcome any rejection made under 35 USC 102 or 103 because the Application does not appear to contain support for the NOD/SCID/IL2rg-null mouse as claimed in the instant amendment, and a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Response & Withdrawn Claim Rejections - 35 USC § 102

Claims 1-5 and 8 were rejected under 35 U.S.C. 102(b) as being anticipated by Ishikawa et al. (Am. J. Transpl. 2:520-525, 2002), in the previous office action dated April 15, 2008. Applicants' cancellation of claim 3 renders its rejection moot. Applicants have amended the claims to recite a NOD/SCID/IL2rg-null mammal; a limitation not taught by Ishikawa et al. Thus, the rejection is hereby withdrawn. Applicants' arguments are considered moot in view of the withdrawn rejection. The claims are however subject to new rejections as outlined below.

Withdrawn Claim Rejections - 35 USC § 103

Claims 1, 6 and 7 were rejected under 35 U.S.C. §103(a) as being unpatentable over Ishikawa et al. (Am. J. Transpl. 2:520-525, 2002), in view of Olive et al. (Immunol. Cell Biol. 76:520-525, 1998), in the previous office action dated April 15, 2008. Applicants have amended the claims to recite a NOD/SCID/IL2rg-null mammal; a limitation not taught by Ishikawa et al. or Olive et al. Thus, the rejection is hereby withdrawn. The claims are however subject to new rejections as outlined below.

Response to Arguments

To the extent that Applicants' arguments may be pertinent to the new rejections set forth below, they are addressed as follows:

Applicants have outlined a number of characteristics for the claimed mammal, presented as items i) to x), as exemplified in Examples 6-10 the specification. Applicants' arguments have been fully considered, but are not found persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. human erythrocytes, megakaryocytes and thrombocytes, CD19+CD20hi mature B cells, CD10+CD19+ immature B cels and CD34+CD19+ pro-B cells, IgM+, IgD+ , IgG+ and IgA+B cells, CD4+CD8+ T cells, human IgA+B cells, human CD3+T cells, human antigen-presenting cells, dendritic cells and monocytes, alloantigen-specific human IgM and IgG and alloantigen-specific human T cells) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants have argued that the mice described by Olive are 8-week old and not newborn. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The mice described by Ishikawa et al. are new-born mice.

Applicants further argue that there is no motivation for a skilled reader of Ishikawa and Olive to replace NOD/SCID/ β2-microglobulin^{null} mice or Hu-PBL-SCID mice with the claimed invention in order to achieve their objective. Such is not found persuasive, because an obviousness rejection need not be based on a strict TSM test, as rationale to support rejections under 358 U.S.C. §103 may include the simple substitution of one known element for another to obtain predictable results.

New Claim Rejections - 35 USC § 103

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 1, 2, 4, 5, 8, 34, 35 and 38 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Ishikawa et al. (Am. J. Transpl. 2:520-525, 2002), in view of mouse strain NOD.Cg-*Prkdc*^{scid}IL2rg^{tm1Wjl}/Sz (Stock No: 00557, Jackson Laboratory).

The claims embrace a newborn NOD/SCID/IL2rg-null mouse into which human cord blood hematopoietic cells have been transplanted, and which is able to generate T cells from said human cells.

Ishikawa et al. describe long-term xenogeneic engrafting of cord blood human hematopoietic cells into newborn NOD/SCID/β2-microglobulin deficient mice (Title and Abstract; limitation of claims 1, 4 8, 34 and 35). Further describing multilineage engraftment, and that high levels of engraftment were primarily by T cells (first column, p. 490 and Figure 1; limitation of claim 5). With reference to previously published results by Kollet et al., the authors additionally state because the duration of engraftment was relatively short, backcrossing onto other strains of mice may be needed for longevity, constituting breeding of the immature immunodeficient mouse (limitation of claim 2).

While Ishikawa et al. do not describe their graft recipient mice as NOD/SCID/IL2rg-null, such was known in the prior art. It should be noted that the instant specification indicates that the NOD/SCID/IL2rg-null mice are NOD.Cg-*Prkdc*^{scid}IL2rg^{tm1Wjl}/Sz, from Jackson Laboratory (Example 6, p. 23).

The product description for stock no. 005557, discloses NOD.Cg-*Prkdc*^{scid}IL2rg^{tm1Wjl}/Sz mice as commercially available from the Jackson Laboratory, and further states that the mice

carry mutations for combined immune deficiency and IL2 receptor gamma deficiency, lack mature T cells, B cells and functional NK cells, leading to better engraftment of human hematopoietic stem cells.

The teachings of Ishikawa et al. and Jackson Laboratory product stock no. 00557 are both directed to engraftment of human hematopoietic cells in immunodeficient mice. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to utilize the NOD/SCID/IL2rg-null mouse in the transplantation assay described by Ishikawa et al. with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would have been motivated to utilize the NOD/SCID/IL2rg-null mouse for engraftment, as a matter of design choice, said design choice amounting to combining prior art elements according to known methods to yield predictable results. Applicants should note that the *KSR* case forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. *KSR International Co. v. Teleflex Inc.*, 550 U.S.-, 82USPQ2d 1385 (2007).

Claims 1, 2, 6, 7, 36 and 37 are rejected under 35 U.S.C. §103(a) as being unpatentable over Ishikawa et al. (Am. J. Transpl. 2:520-525, 2002), in view of mouse strain NOD.Cg-*Prkdc*^{scid}IL2rg^{tm1Wjl}/Sz (Stock No: 00557, Jackson Laboratory), as applied to claims 1, 2, 4, 5, 8, 34, 35 and 38 above, and further in view of Olive et al. (Immunol. Cell Biol. 76:520-525, 1998).

The claims embrace a newborn NOD/SCID/IL2rg-null mouse into which mature human hematopoietic cells have been transplanted, and which is able to generate IgG immunoglobulin from said human cells.

Ishikawa et al. teach long-term xenogeneic engrafting of cord blood human hematopoietic cells into newborn NOD/SCID/β2-microglobulin deficient mice (Title and Abstract). Further teaching multilineage engraftment, that included cells bearing the CD19 pan-specific B cell marker (Table 1, p. 492). The product description for stock no. 005557, discloses NOD.Cg-*Prkdc*^{scid}IL2rg^{tm1Wjl}/Sz mice as commercially available from the Jackson Laboratory

While neither Ishikawa et al. or Jackson Laboratory product description for stock no. 005557 describe detecting IgG in the recipient newborn mice, the production of human IgG in

xenografted immunodeficient mice was well known in the prior art. Olive et al. describe the successful engraftment of human peripheral blood lymphocytes in SCID mice, determined by measurement of human IgG in mouse sera, that continued to increase for 8 weeks, in addition to T cell engraftment in lymphoid tissues (Title and Abstract; limitation of claims 6, 7, 36 and 37); thus curing the deficiency of IgG in Ishikawa et al. and product no. 005557

Ishikawa et al. state that the number of cells that were planted per newborn mouse is less than the larger graft size previously reported in earlier studies (second column, p. 493), thus providing the motivation to use newborn mice instead of the 8 week old mice utilized by Olive et al.

The teachings of Ishikawa et al., product stock no. 005557 and Olive et al. are all directed to engraftment of human hematopoietic cells in immunodeficient mice. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine their respective teachings and to introduce human hematopoietic cells into newborn NOD/SCID/IL2rg-null mice to produce human T cells and IgG, with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would be motivated to use the newborn immunodeficient mouse of Ishikawa et al. for human hematopoietic cell engraftment, because such would require a smaller graft size.

Conclusion

Claims 1, 2, 4-8 and 34-38 are not allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. The claims are drawn to the same invention claimed earlier in the application and would have been finally rejected on the grounds and art of record in the next Office Action if they had been entered earlier in the application. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Examiner, Art Unit 1633